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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/534,544

05/10/2005

Shmuel Pietrokovski

29489

7801

67801

7590

12/18/2008

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EXAMINER

OGUNBIYI, OLUWATOSIN A

ART UNIT

PAPER NUMBER

1645

MAIL DATE

DELIVERY MODE

12/18/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/534,544	Applicant(s) PIETROKOVSKI ET AL.	
	Examiner OLUWATOSIN OGUNBIYI	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 September 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 5-121 is/are pending in the application.
- 4a) Of the above claim(s) 19-121 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 5-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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RESPONSE TO AMENDMENT

The amendment filed 9/11/08 has been entered into the record. Claims 2-4 have been cancelled. Claims 1, 5- 121 are pending. Claims 1 and 5-18 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Objections/Rejections Withdrawn

The objection to claims 1-4 and 6 are withdrawn in view of the cancellation of claims 2-4 and the amendment to claim 1 and 6.

The rejection of claims 1-18 under 35 U.S.C. 112, first paragraph (scope of enablement) is withdrawn in view of the amendment to the claims.

The rejection of claims 1-15 under 35 U.S.C. 112, second paragraph is withdrawn in view of the amendment to the claims.

Claims 1-12 and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Chong et al The Journal of Biological Chemistry vol. 271:22159-22168, 1996 (IDS) is withdrawn in view of the amendment to the claims.

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Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chong et al The Journal of Biological Chemistry vol. 271:22159-22168, 1996 (IDS) is withdrawn in view of the amendment to the claims.

The rejection of claims 16 and 18 under 35 U.S.C. 103(a) as being unpatentable over Chong et al The Journal of Biological Chemistry vol. 271:22159-22168, 1996 as applied to claims 1-12 and 14-17 in view of Jarvik et al Anu. Rev. Genet. 1998, 32:601-18 is withdrawn in view of the amendment to the claims.

The rejection of claims 16 and 17 under 35 U.S.C. 103(a) as being unpatentable over Chong et al The Journal of Biological Chemistry vol. 271:22159-22168, 1996 as applied to claims 1-12 and 14-17 in view of Chong et al Nucleic Acids Research, 1998 vol. 26: 5109-5115 (IDS) is withdrawn in view of the amendment to the claims.

Rejections Maintained

The rejection of claims 16-18 under 35 U.S.C. 112, second paragraph is maintained.

The claims are drawn to the chimeric polypeptide of claim 1 further comprising an affinity tag capable of specifically binding a molecule wherein the molecule forms a part of a virus or a cell. Applicant argues that affinity tags are well known for purification of cells, viruses and molecules and the like. This is not found persuasive. The claims are vague and indefinite as

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to which part of a virus or a cell the affinity tag binds to. Affinity tags are known in the art for purifying proteins that have been engineered to comprise such affinity tags which binds its binding partner. For example, a protein is engineered to have maltose binding protein (MBP) as the affinity tag and the protein is purified on the affinity column comprising amylose which binds the MBP-protein fusion. In the instant case the specification does not disclose specific examples of affinity tags that can bind substrates/molecules that *forms part of* a virus or cell to. Jarvik et al Anu. Rev. Genet. 1998, 32:601-18, cited previously teaches that *affinity tags can be derived from* viruses and human cells (p. 604 table 1). The art does not teach an affinity tag that specifically binds viruses and cells including binding molecules that forms part of a virus or cell. Specific examples of what is meant by this limitation would further help to clarify this issue in the claims.

New Rejections Based on Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new matter rejection.

The amended claim is now drawn to a chimeric polypeptide comprising an autoproducting segment having *the* amino acid sequence set forth by SEQ ID NO: 31 further comprising an affinity tag capable of specifically binding a molecule wherein said molecule forms a part of a virus or a cell. The claim as amended encompasses new matter as the specification as filed does not provide support for the binding a molecule wherein said molecule forms a part of a virus or a cell. *Emphasis added.* Applicant is required to cancel the new matter or other appropriate action such as by pointing to the specification by page and line number for support for the claim as amended.

Claims 1 and 5-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims as amended are now drawn to a chimeric polypeptide comprising an autoproducting segment having *the* amino acid sequence set forth by SEQ ID NO: 31.

The specification sets forth the sequence for SEQ ID NO: 31 (BIL4_CLOTH) as follows:

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<210> 31
 <211> 136
 <212> PRT
 <213> Clostridium thermocellum

<220>
 <221> misc_feature
 <222> {36}..{57}
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> {73}..{76}
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> {106}..{111}
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> {127}..{128}
 <223> Xaa can be any naturally occurring amino acid

<400> 31

Cys Phe Val Ala Gly Thr Met Ile Leu Thr Ala Thr Gly Leu Val Ala
 1 5 10 15

Ile Glu Asn Ile Lys Ala Gly Asp Lys Val Ile Ala Thr Asn Pro Glu
 20 25 30

Thr Phe Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 35 40 45

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly Gly Glu Val Ile Lys Thr
 50 55 60

Thr Phe Asp His Pro Phe Tyr Val Xaa Xaa Xaa Xaa Phe Val Glu Ala
 65 70 75 80

Gly Lys Leu Gln Val Gly Asp Lys Leu Leu Asp Ser Arg Gly Asn Val
 85 90 95

Leu Val Val Glu Glu Lys Lys Leu Glu Xaa Xaa Xaa Xaa Xaa Xaa Lys
 100 105 110

Val Tyr Asn Phe Lys Val Asp Asp Phe His Thr Tyr His Val Xaa Xaa
 115 120 125

Asn Glu Val Leu Val His Asn Ala
 130 135

The sequence set forth above for SEQ ID NO: 31 encompasses an extremely large number of different species because of the variability allowed in the sequence - 4 domains (intervening sequences) of the sequence above have regions of variability i.e. Xaa can be any naturally amino acid sequence and there 20 possible amino acid choices for each Xaa position.

The specification teaches in example 4 page 56 that a chimeric protein which comprises the type A BIL domain BIL4_cloth (SEQ ID NO: 31) has the capacity to efficiently display auto-splicing and carboxy terminal auto-cleaving activity. Hence such a BIL domain can therefore be advantageously exploited in applications benefiting from an auto-splicing and/or carboxy terminal auto-cleaving chimeric protein (see conclusion to example 4 experiment on p. 57 lines 5-9).

The specification in example 4 does not set forth which species was used for the experiment - the designation of BIL4-cloth in example 4 does not set forth which variant and its sequence including the particular sequence of the variable regions was used in the auto-splicing and c-terminal cleavage of example 4. It is well known in the art that amino acid substitutions anywhere protein's sequence including in areas not required for activity can affect the protein's structure and thus its function (Ng et al. Genome Research 2001 May; 11 (5): 863-874); Bowie et al. Science Vol. 247, No. 4948, p. 1306-1310, 1990; Lazar et al. Molecular and Cellular Biology, Mar. 1988, p. 1247-1252 and Burgess et al. The Journal of Cell Biology, vol. 111, Nov. 1990 2129-2138.

In such an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See *Noelle v Lederman*, 355 F. 3d 1343, 1350, 69 USPQ2d 1508, 1514 (*Fed. Cir. 2004*) and *In re Alonso* (Fed. Cir. 2008-1079). In the instant case, the specification does not disclose even one species of the extremely large genus to which the claims are drawn. The disclosure of SEQ ID NO: 31 which comprise intervening sequences which can have any amino acid sequence does not adequately describe the genus comprises the plethora of different species. The specification does not

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disclose at least one species that can auto-splice and has c-terminal cleaving activity and because of the effects amino acid changes even in areas not required for activity can have on a protein's structure (thus its function) – it is impossible to predict which of these variants can auto-process and which cannot.

Therefore, in view of the above considerations, one of skill in the art would not recognize that Applicants were in possession of the variants encompassed in SEQ ID NO: 31 that have autoprocessing activity.

Claims 1 and 5-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims as amended are now drawn to a chimeric polypeptide comprising an autoprocessing segment having *the* amino acid sequence set forth by SEQ ID NO: 31.

The specification sets forth the sequence for SEQ ID NO: 31 (BIL4_CLOTH) as follows:

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<210> 31
 <211> 136
 <212> PRT
 <213> Clostridium thermocellum

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 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> {106}..{111}
 <223> Xaa can be any naturally occurring amino acid

<220>
 <221> misc_feature
 <222> {127}..{128}
 <223> Xaa can be any naturally occurring amino acid

<400> 31

Cys Phe Val Ala Gly Thr Met Ile Leu Thr Ala Thr Gly Leu Val Ala
 1 5 10 15

Ile Glu Asn Ile Lys Ala Gly Asp Lys Val Ile Ala Thr Asn Pro Glu
 20 25 30

Thr Phe Glu Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 35 40 45

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gly Gly Glu Val Ile Lys Thr
 50 55 60

Thr Phe Asp His Pro Phe Tyr Val Xaa Xaa Xaa Xaa Phe Val Glu Ala
 65 70 75 80

Gly Lys Leu Gln Val Gly Asp Lys Leu Leu Asp Ser Arg Gly Asn Val
 85 90 95

Leu Val Val Glu Glu Lys Lys Leu Glu Xaa Xaa Xaa Xaa Xaa Xaa Lys
 100 105 110

Val Tyr Asn Phe Lys Val Asp Asp Phe His Thr Tyr His Val Xaa Xaa
 115 120 125

Asn Glu Val Leu Val His Asn Ala
 130 135

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The specification teaches in example 4 page 56 that a chimeric protein which comprises the type A BIL domain BIL4_cloth (SEQ ID NO: 31) has the capacity to efficiently display auto-splicing and carboxy terminal auto-cleaving activity. Hence such a BIL domain can therefore be advantageously exploited in applications benefiting from an auto-splicing and/or carboxy terminal auto-cleaving chimeric protein (see conclusion to example 4 experiment on p. 57 lines 5-9). T

The sequence set forth above for SEQ ID NO: 31 encompasses an extremely large number of different species because of the variability allowed in the sequence - 4 domains (intervening sequences) of the sequence above have regions of variability i.e. Xaa can be any naturally amino acid sequence and there 20 possible amino acid choices for each Xaa position.. The specification in example 4 does not set forth which species was used for the experiment - the designation of BIL4-cloth in example 4 does not set forth which variant and its sequence was used in the auto-splicing and c-terminal cleavage of example 4. It is well known in the art that amino acid substitutions anywhere protein's sequence including in areas not required for activity can affects the protein's structure and thus its function. See Ng et al. Genome Research 2001 May; 11 (5): 863-874; Bowie et al. Science Vol. 247, No. 4948, p. 1306-1310,1990; Lazar et al. Molecular and Cellular Biology, Mar. 1988, p. 1247-1252 and Burgess et al. The Journal of Cell Biology, vol. 111, Nov. 1990 2129-2138. The specification does not set forth the sequence of the 4 intervening sequences used for the BIL4-cloth used in the experiment of example 4 and it is unpredictable to one of skill in the art which of the plethora of variable intervening sequence will or will not have effect on the structure of the protein thus having an effect on its activity to auto-process. Therefore, undue experimentation would be required of the skilled artisan to make and use the instant invention as there is no information on which variant intervening sequence will not affect the structure and thus the function of the autoprocessing segment.

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Claim 10 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 depends from claim 5 and recites the limitation "wherein said segment of the polypeptide adjacent to said amino terminal end of said autoproducting segment". There is insufficient antecedent basis for this limitation in the claim. There are two polypeptides in claim 5 - the autoproducting segment and the 'first polypeptide'. In claim 10 which polypeptide is being referred to? Also, 'segment of the polypeptide adjacent to said amino terminal end of said autoproducting segment' lacks antecedent basis because claim 5 recites *carboxy terminal* not *amino terminal*.

Status of Claims

Claims 1 and 5-18 are rejected. No claims allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action

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is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am- 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Oluwatosin Ogunbiyi/

Examiner, Art Unit 1645

/Robert B Mondesi/

Supervisory Patent Examiner,

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